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SMITHKLINE BEECHAM CORPORATION  
CORPORATE INTELLECTUAL PROPERTY-US, UW2220  
P. O. BOX 1539  
KING OF PRUSSIA, PA 19406-0939

EXAMINER

KERR, KATHLEEN M

ART UNIT PAPER NUMBER

1652

DATE MAILED: 06/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/743,209

Applicant(s)

BARTON ET AL.

Examiner

Kathleen M Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 31 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 15-28 is/are pending in the application.
- 4a) Of the above claim(s) 21,22 and 24-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15-20 and 23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Application Status***

1. In response to the previous Office action, a non-Final rejection (Paper No. 16, mailed on November 19, 2002), Applicants filed an amendment and response received on March 31, 2003 (Paper No. 18). Said amendment amended Claims 15, 16, and 19. Thus, Claims 15-28 are pending in the instant Office action.

### ***Election***

2. Claims 15-28 are pending in the instant application. Claims 21, 22, and 24-28 are withdrawn from further consideration as non-elected inventions. Claims 15-20 and 23 will be examined herein.

### ***Priority***

3. As previously noted, the instant application is 371 application of International Application No. PCT/GB99/02301 filed on July 15, 1999 and is granted the benefit of priority for the foreign application 9815666.4 filed in the Great Britain on July 17, 1998.

### ***Sequence Compliance***

4. By virtue of Applicant's amendment to the specification to identify all sequences in the specification with a SEQ ID NO identifier, the instant application now fully complies with the sequence rules.

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***Withdrawn - Objections to the Specification***

5. Previous objection to the instant specification because it does not contain an abstract of the disclosure as required by 37 C.F.R. § 1.72(b) is withdrawn by virtue of Applicants' filing an abstract.
6. Previous objection to the specification for having an unclear copy is withdrawn by virtue of Applicant's amendment.
7. Previous objection to the specification for being confusing with respect to the sequence listing is withdrawn by virtue of Applicants' amendment to the specification.

***Withdrawn - Claim Objections***

8. Previous objection to Claim 19 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicants' amendment.

***Maintained - Claim Objections***

9. Previous objection to Claim 23 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is maintained. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants argue that "the limitations of claim 23 reciting that the polypeptide is obtained from a recombinant vector is proper". Without further explanation of Applicants' reasoning, this argument cannot be addressed adequately except to be reiterated. Applicants should cite *how* the recombinant production of a polypeptide further limits the nature of the polypeptide used in the

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methods of the parent claim since, as previously noted, "The manner in which the polypeptide used in Claims 15 or 16 was obtained does not effectively further limit the polypeptide obtained. In other words, the polypeptide used in Claim 15 is the same if purified from a natural source or if expressed via the vector system as prescribed in Claim 23. Thus, the additional requirement on how the protein is produced has no real effect on the nature of the protein product itself."

***Withdrawn - Claim Rejections - 35 U.S.C. § 101***

10. Previous rejection of Claims 15-20 and 23 under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter is withdrawn by virtue of Applicants' amendment.

***Withdrawn - Claim Rejections - 35 U.S.C. § 102***

11. Previous rejection of Claims 15-20 and 23 under 35 U.S.C. § 102(b) as being anticipated by Baggaley *et al.* as evidenced by Jensen *et al.* is withdrawn, as previously applied, by virtue of Applicants' amendment. However, an analogous new rejection is set forth below. Applicants argue that Baggaley *et al.* do not teach an "isolated" enzyme related to SEQ ID NO:2 and that Jensen *et al.* do not teach the function of SEQ ID NO:2 as it is disclosed. The rejection below notes that Baggaley *et al.*, in fact, do teach using an isolated enzyme (see noted citation).

**NEW OBJECTIONS/REJECTIONS**

***Objections to the Specification***

12. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in

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foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the source species, *Streptomyces clavuligerus*, for completeness.

### ***Claim Objections***

13. Claim 19 is objected to for having improper English. The phrase "native to *Streptomyces* species" is improper since there are numerous *Streptomyces* species. The Examiner suggests using ---native to a *Streptomyces* species--- (emphasis added) for proper form.

### ***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 15-20 and 23 are rejected under 35 U.S.C. § 102(b) as being anticipated by Baggaley *et al.* (WO 94/12654, see IDS). The instant claims are drawn to methods of making formula IV (see Claim 16) by contacting SEQ ID NO:2, an enzyme from *Streptomyces clavuligerus*, with formula III (N<sup>2</sup>-(2-carboxyethyl)-(S)-arginine). The Examiner notes that when R=H and when R<sup>1</sup>=the left compound (see Claim 15), formula II equals formula III i.e., Claim 16 is a species of Claim 15.

Baggaley *et al.* teach the biosynthetic route producing clavulanic acid in *Streptomyces clavuligerus* (see page 1 and Figure 1). This route includes Applicants' formulas III and IV as

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shown in structure 'A' and 'B', respectively, in Figure 1 of Baggaley *et al.* This route contacts formula III (structure 'A') with an enzyme represented by the arrow labeled "b" in Figure 1 of Baggaley *et al.* to produce formula IV (structure 'B'). Additionally, Baggaley *et al.* teach using a free enzymatic system in contact with formula III (structure 'A') (see page 8, lines 1-4). This enzymatic system, at its most basic level that is fully enabled by the specification of Baggaley *et al.*, can be as simple as a whole cell extract.

While Baggaley *et al.* do not teach the sequence of the protein used as SEQ ID NO:2, the sequence of a protein is an **inherent feature** and need not be specifically described in sequence form providing that the source, in this case *S. clavuligerus*, is the same.

#### ***Allowable Subject Matter***

15. The following is reiterated from the previous Office action and amended below:

"The Examiner notes that although the clavulanic acid biosynthetic pathway route, including formulas III and IV, is taught in the prior art (WO 94/12654) and although the biosynthetic gene cluster from *S. clavuligerus* encoding enzymes, including SEQ ID NO:2, that are necessary and sufficient for producing clavulanic acid is taught in the prior art (CA 2108113), no combination of the prior art teaches that SEQ ID NO:2 catalyzes the reaction converting formula III into formula IV. Thus, the contacting of formula III, *ex vivo*, with, for example, purified SEQ ID NO:2 is neither taught nor obvious in the teachings of the prior art."

The Examiner is herein reconsidering the view of allowable subject matter as previously noted. By virtue of the citation noted above (see art rejection) in Baggaley *et al.* (WO 94/12654), the prior art **does** teach the claimed invention using isolated enzyme. Since the enzyme taught by Baggaley *et al.* is from the same source as SEQ ID NO:2 in the instant application, the enzyme of Baggaley *et al.* inherently has the same structure as required in the claims even though the sequence had not been determined by Baggaley *et al.* Thus, Baggaley *et al.* anticipate all the

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instant claims because all the limitations of Claims 15-20 and 23 are taught when the sequence limitation is an inherent feature of the enzyme.

The Examiner notes, however, that claims drawn to a method using steps of (1) producing an enzyme having the sequence shown in SEQ ID NO:2 in a host cell using a vector comprising **SEQ ID NO:1**, and (2) contacting formula II or III with said enzyme to prepare compound I or IV is neither anticipated nor made obvious by the prior art. The Examiner specifically notes that the production of the protein in a host cell must be an *explicit step*, and not implicit as found in pending Claim 23. While Baggailey *et al.* do teach the isolated protein, they do not teach the isolated DNA encoding said protein, without or without sequence information. Thus, methods using the DNA are not anticipated or rendered obvious by explicit sequence disclosure or by isolation of an "unsequenced" product. Therefore, claims drawn to using the DNA that is SEQ ID NO:1 cannot be anticipated or rendered obvious by Baggailey *et al.*

Additionally, the Examiner reiterates that SEQ ID NOs: 1 and 2 are not novel in the art based on the disclosure of Jensen. However, in Jensen, no function is assigned to the protein. Thus, no motivation to combine SEQ ID NO:2 with any particular substrate can be set forth. Therefore, Jensen does not strengthen the above art rejection because knowing the sequence of the protein is not relevant against the claims as pending.

### ***Summary of Pending Issues***

16. The following is a summary of the issues pending in the instant application:

- a) The Abstract stands objected to for not completely describing the disclosed subject matter.
- b) Claim 19 stands objected to for having improper English.
- c) Claim 23 stands objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form.
- d) Claims 15-20 and 23 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Baggailey *et al.*



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*Conclusion*

17. Claims 15-20 and 23 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

The instant Office action is **non-Final** based on a reconsideration of allowable subject matter and a new version of the previously set forth art rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK

June 9, 2003

